

1      Claims

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3      1. A method for synthesising a given peptide or

4      its derivative which contains a proline

5      residue or a proline derivative, at proximity

6      to, or at, the C-terminal end of said peptide,

7      the method comprising the steps of:

8      a) synthesising on a first resin a C-

9      terminal portion of said peptide, or its

10     derivative, comprising at least three

11     successive amino acid residues or their

12     derivatives, by successive coupling of

13     selected amino acids, small peptides or

14     their derivatives, said first resin being

15     suitable for the formation of peptides

16     having a proline residue or a proline

17     derivative positioned at, or at proximity

18     of, the C-terminal end of said peptide;

19     b) cleaving the C-terminal portion thus

20     obtained from said first resin;

21     c) reattaching said C-terminal portion to a

22     second resin which is generally suitable

23     for the synthesis of peptides but is

24     unsuitable for the formation of peptides

25     having a proline residue or a proline

26     derivative positioned at, or at proximity

27     of, the C-terminal end of said peptide;

28     and

29     d) coupling selected amino acids, small

30     peptides or derivatives to the C-terminal

31     portion to obtain said given peptide.

1       2. The method of Claim 1 wherein said peptide is  
2       a long peptide.

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4       3. The method of Claim 1 or 2 wherein said given  
5       peptide is a chemokine having a proline  
6       residue or a proline derivative at the C-  
7       terminal or at proximity thereof.

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9       4. The method of any one of Claims 1 to 3,  
10      wherein said first resin is chosen so that it  
11      does not lead to the formation of cyclic  
12      dipeptide and in particular diketopiperazine  
13      compounds.

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15      5. The method of any one of Claims 1 or 4,  
16      wherein said step a) and/or d) is achieved by  
17      successive coupling of the predetermined amino  
18      acid residues or derivatives.

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20      6. The method of any one of Claims 1 to 5,  
21      wherein said first resin for the formation of  
22      the C-terminal portion is the 2-chlorotriptyl  
23      chloride resin.

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25      7. The method of any one of Claims 1 to 6,  
26      wherein said second resin is a resin of the  
27      type having benzyl ester linkers.

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29      8. The method of any one of Claims 1 to 7,  
30      wherein said second resin is a Wang type  
31      resin.

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1       9.   The method of any one of Claims 1 to 8,  
2       wherein said given peptide as up to 150 amino  
3       acid residues.

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5       10.   The method of any one of Claims 1 to 9,  
6       wherein the cleaving step is achieved using a  
7       mild acid treatment, for example 20%  
8       trifluoroethanol in dichloromethane.

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10      11.   The method of any one of Claims 1 to 10,  
11      wherein the C-terminal portion is fully  
12      protected so it can be attached directly onto  
13      the second resin.

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